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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/936,823	10/24/2001	Merja Penttila	0933-0170P	1523

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EXAMINER

LIU, SAMUEL W

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 01/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/936,823

Applicant(s)

PENTTILA ET AL.

Examiner

Samuel W Liu

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 16 November 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1 and 3-25 is/are pending in the application.
- 4a) Of the above claim(s) 6-9, 16, 17 and 24 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1, 3-5, 10-15, 18-23 and 25-27 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date: _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date: _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Status of the claims

Claims 1 and 3-25 are pending.

Applicants' amendment filed 16 November 2004, which amends claims 1, 6, 9-12, 14-24, and adds claims 25-27 has been entered. Claims 6-9, 16-17 and 24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention (see the Office action mailed 16 June 2004). Claims 6-9, 16-17 and 24 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Note that claim 2 is canceled by the applicants' amendment filed 6 May 2004.

Thus, the pending claims 1, 3-5, 10-15, 18-23 and 25-27 are examined in this Office action.

Please note that grounds of objection and/or rejection not explicitly restated and/or set forth below are withdrawn.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter that the applicant regards as his invention.

Claims 1, 3-5, 10-15, 18-23 and 25-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim is indefinite in recitation (*item a*) "a target protein ... having the ability to partition in ATPS and to carry said (fusion) protein or cell" and recitation "said fusion protein or cell carrying the targeting protein" (*item b*); because it is paradoxical that how the target protein is a

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carrier that carries the fusion protein or cell meanwhile said target protein is carried by said fusion protein or cell. Clarification in this regard is required therefore. Further, claim 1, item *b*, recites "... said fusion protein or cell carrying the targeting protein..."; the recitation appears to be unclear because, according to the claimed subject matter of claim 1, it is the target protein that mediates (i.e., carries) the protein or the cell of interest to be partitioning in ATPS; yet, it would be inappropriate vice versa. The dependent claims are also rejected.

Claim 10 is indefinite because claim 10 (a composition claim) depends from claim 3 (a process claim); this claim dependency is improper and renders the claim indefinite. The dependent claims are also rejected.

Claim 15 is indefinite because of its multiple claim dependency, i.e., claim 5 depends from claims 1 and 10. This improper claim dependency renders claim 15 indefinite. Note that claim 15, which is a process claim, should not depend from claim 10, which is a composition claim. Writing the claim in proper claim dependency thus is required.

Claim 19 is indefinite because claim 19 (a process claim) depends from claim 10 (a composition claim); this claim dependency is improper and renders the claim indefinite. The dependent claims are also rejected.

Claim Rejections - 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

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Claims 1, 5, 20 and 23 are rejected under 35 U.S.C. 102(b) as being anticipated by Kohler, K. et al. (*Bio/tech.* (1991) 9, 642-646).

Kohler et al. teach a method of separating of proteins in an aqueous two-phase system (ATPS) comprising (i) preparing a fusion polypeptide comprising part of hydrophobin-like protein (i.e., tryptophan-rich oligopeptide (e.g., Ala-Trp-Trp-Pro)) and protein of interest, and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. Since claim 1 language sets forth “hydrophobin-like proteins and parts thereof” wherein the “parts” of the “hydrophobin-like proteins”, as written, would encompass any peptides or proteins which behavior like hydrophobin and have a high partitioning coefficient in hydrophobic phase of the ATPS. Thus, the Kohler et al. teaching anticipates the instant claim 1.

Since in the aqueous solution, the said oligopeptide is highly hydrophobic and tends to aggregate, and since this ability of the aggregation in the solution is an inherent property of the oligopeptide, the above Kohler et al. teaching anticipates the instant claim 5.

Also, Kohler et al. teach the said ATPS is PEG/salt system (see abstract and page 646, “*Portioning experiment*”), which anticipates the instant claim 20.

Also, Kohler et al. teach that, prior to applying the sample containing fusion protein that comprises protein to be separated (of interest), the solution comprising the expressed fusion protein is subject to a chromatography in order to separate the solution from cell extract which expresses the fusion protein thereof; and then, the sample solution comprising the fusion protein is subjected to partitioning in PEG/salt aqueous two-phase system (see pages 643-644), which anticipates the instant claim 23.

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The applicants' response to the rejection under 35 USC 102(b)

The response filed 16 November 2004 discuss the Kohler's oligopeptide comprising tryptophans; argues that the hydrophobin do not usually contain tryptophan; and thus, infers that the Kolher's teachings do not anticipate the current invention (see page 18, the 2nd paragraph and page 19). The applicants' argument is found to be unpersuasive because (i) page 7, line 28 (applicants refer to this page for their argument) of the specification does not absolutely rule out that hydrophobin contain tryptophan (Trp) as is evidenced by the reference (Tagu, D. et al. (1996) Gene, 168, 93-97) which shows that a hydrophobin protein comprises Trp residue (see Figure 1 (A)); and (ii) the claims as written is also directed to hydrophobin-like protein or/and parts thereof which would encompass any proteins or peptides capable of being efficiently partitioning in the ATPS' phase, e.g., the Kohler's oligopeptide regardless of their amino acid composition containing Trp or not. Note that the independent claim 1 as written does not specifically set forth that the claimed protein contains no tryptophan residue(s). Thus, the rejected stated above is maintained.

The following is the new ground of rejection

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various

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claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kohler, K. et al. (*Bio/tech.* (1991) 9, 642-646) taken with Liu, C.-L. et al. (*J. Chromatog.* (1998) 711, 127-138) and in view of the “reference 1” (see attachment).

Kohler et al. teach a method of separating of proteins in an aqueous two-phase system (ATPS) comprising (i) preparing a fusion polypeptide comprising part of hydrophobin-like protein (i.e., tryptophan-rich oligopeptide (e.g., Ala-Trp-Trp-Pro)) and protein of interest, and (ii) subjecting said fusion protein to the ATPS-mediated protein separation. Since claim 1 language sets forth “hydrophobin-like proteins and parts thereof” wherein the “parts” of the “hydrophobin-like proteins”, as written, would encompass any peptides or proteins which behavior like hydrophobin and have a high partitioning coefficient in hydrophobic phase of the ATPS. Thus, the Kohler et al. teaching is applied to the instant claim 1.

Also, Kohler et al. teach the said ATPS is PEG/salt system (see abstract and page 646, “*Portioning experiment*”), as applied to the instant claims 20-21.

Kohler et al. do not expressly teach that the ATPS comprises a detergent.

Liu et al. teach separation of protein using the ATPS which comprises nonionic surfactant (see abstract), as applied to the instant claim 21. Note that surfactants constitute the most important group of detergent components (see page 1 of the attachment labeled “reference 1”).

It would be obvious to one of ordinary skill in the art at the time the invention was made to combine the Kohler and Liu teachings so as to develop a detergent-based aqueous two-phase system for separating recombinantly produced proteins or polypeptides because it offers the following obvious advantages, as taught by Liu et al. (1) nonionic surfactant provides a mild and friendly environment to biomolecules and does not denature proteins (see page 128, the right column, the 2nd paragraph); (2) the nonionic surfactant self-assembles in solution as micelles which enables one to easily control and optimize the partitioning behavior by tuning micellar characteristics (see page 129, the right column, the 3rd paragraph); (3) allow the partitioning to be selective through formulating affinity ligand into the micelles, which renders the protein to be separated biospecific (page 129, the right column, the 5th and 6th paragraphs); and (4) removal of micelles from the desired biomolecules after partitioning can be facilitated by self-assembling feature of the micelles (see page 130, the left column, the 1st paragraph).

Given the above motivations, one of ordinary skill in the art would have incorporated surfactant (detergent) in the ATPS for efficient separation/purification of protein of interest; and thus, would have readily arrived at the current invention with successful expectation.

Therefore, the claimed invention was *prima facie* obvious to make and use the invention at the time it was made.

Conclusion

No claims are allowed.

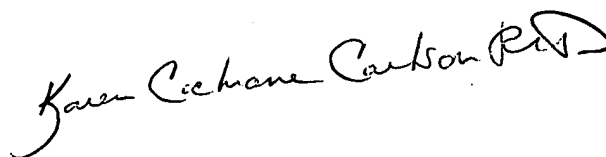
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Samuel Wei Liu whose telephone number is 571-272-0949. The examiner can normally be reached from 9:00 a.m. to 5:00 p.m. on weekdays. If attempts to reach

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the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Christopher Low, can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703 308-4242 or 703 872-9306 (official) or 703 872-9307 (after final). Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703 305-4700.



Samuel Wei Liu, Ph.D.
Art Unit 1653, Examiner
December 7, 2004



KAREN COCHRANE CARLSON, PH.D.
PRIMARY EXAMINER